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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,666	02/15/2002	Tsuneji Suzuki	054160-5060	7720

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MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1615	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/049,666	SUZUKI ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response dated 12-4-06 is acknowledged.

Claims included in the prosecution are 44-49.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this office action'.

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 44-49 are rejected under 35 U.S.C. l03 (a) as being unpatentable over EP 0847 992 (Suzuki et al).

EP teaches benzamide derivative claimed by applicant (see claim 14). Additionally, EP teaches that the active ingredient may be used in general pharmaceutical compositions, and may be prepared with generally used diluents or excipients, such as binders, extenders, fillers, moisturizers, disintegrants, surfactants, and lubricants. EP also teaches that the pharmaceutical dosage form can be a tablet, pill, powder, solution, suspension, emulsion, granules, capsule, injection or suppository. More specifically, EP teaches the use of calcium carbonate, amino acids, starch, methyl

celluloses, calcium Carmellose, lactose, sugars, stearates, talc, polyethylene glycol, sodium alginate and many other well known excipients (page 46, lines 5- 39). The use of these excipients in combination with claimed benzamide derivative would have been obvious to one of ordinary skill in the art with a reasonable expectation of success, since EP is suggestive of these art known excipients together with the benzamide derivative.

3. Claims 44-49 are rejected under 35 U.S.C. l03 (a) as being unpatentable over EP 0847 992 in view of the International Cosmetic Ingredient Dictionary and Handbook.

EP described above as teaching pharmaceutical compositions comprising benzamide derivatives. EP teaches the inclusion of many well-known pharmaceutical excipients. EP does not teach the inclusion of each of the specific excipients claimed by Applicant. EP does not specifically teach mannitol or claimed amino compound or organic and inorganic salts. The International Cosmetic Ingredient Dictionary and Handbook is relied upon for the teachings that mannitol as well known binder. Lastly, the Dictionary and Handbook is relied upon for the teaching that inorganic compounds such as sodium bicarbonate, disodium phosphate, potassium bicarbonate and ammonia, as well as amino compounds such as triethanolamine, diethanolamine, diisopropanolamine, and triisopropanolamine, as well as organic acid salts such as sodium fumarate, and trisodium phosphate are all well known pH adjusters. Each of these types of excipients (binders, film formers and pH adjusters) is well known excipients used in the making of pharmaceutical formulations. Therefore, their inclusion in a pharmaceutical composition, which allows for necessary excipients, is not found to

be patentable. The selection of a known material based on its suitability for its intended use is obvious, absent a clear showing of unexpected results attributable to the Applicant's specific selection. One skilled in the art would have been motivated to include the well-known excipients discussed above in the compositions described by EP with a reasonable expectation of success. The motivation to do so lies in the teaching of EP that well known excipients can be included in their formulation. Adjusting the pH of a composition is deemed to be within the skill of the art since that is routinely practiced in the fields of Chemistry and Biochemistry. The criticality of the product produced by dry granulation is unclear since one of ordinary skill in the art would avoid wet granulation process if the moisture leads to the degradation of the active agent. Therefore, this invention as a whole would have been prima-facie obvious to one of ordinary skill in the art at the time the invention was made.

4. Claims 44-49 are rejected under 35 U.S.C. 103 (a) as being unpatentable over EP 0847 992 combination with Savastano (5,681,584).

The teachings of EP have been discussed above. EP does not specifically teach excipients such as pregelatinized starch, mannitol, amino acids such as glycine, inorganic salts such as disodium phosphate.

Savastano while disclosing tablet formulations of Benzamide derivatives suggests that excipients such as pregelatinized starch, mannitol, amino acids such as glycine, and inorganic salts such as disodium phosphate be used (col. 7, line 4 through col. 8, line 65).

It would have been obvious to use these excipients in the compositions of EP would have been obvious to one of ordinary skill in the art with a reasonable expectation of success since the reference of Savastano is suggestive of the use of these excipients with other benzamide derivatives. As pointed out above, adjusting the pH of the composition with acids and bases to obtain the desired pH at which the benzamide derivatives are fully active without degradation is well within the skill of the art.

Applicant's arguments based on the declaration by Masahiro Sakabe have been fully considered, but are not found to be persuasive. In his declaration, Masahiro Sakabe argues that he believes that an artisan skilled in the art of high-performance liquid chromatography (HPLC), the differences between the listed numbers are statistically significant. According to Sakabe Table 1 shows that when D-mannitol and compound I are mixed together and subjected to the indicated conditions, compound 1 is degraded by 0.21 percent (%) relative to the total amount of compound I present in the mixture and this value is comparable to the stability of compound 1 in the absence of any additional component (0.18 or 0.19 depending on the conditions tested). Further according to Sakabe in contrast, when lactose and compound I are mixed together and subjected to the indicated conditions, compound 1 is degraded by 0.55 percent (%) or 0.44 % relative to the total amount of compound 1 present in the mixture, depending on the particular conditions tested. Finally, Sakabe states that given his level of skill in HPLC chromatography, he believe that the difference between, for example, 0.21 (D-mannitol + compound 1) and 0.55 or 0.44 (lactose + compound 1) is statistically significant in that a conclusion may be drawn regarding the stabilizing effects of D-

mannitol on compound 1 and the destabilizing effects of lactose on compound I. These arguments are not persuasive. The examiner is not questioning the level of skill of Masahiro Sakabe with regard to HPLC. What Masahiro Sakabe is offering is his opinion with regard to Statistics, which is totally different from HPLC results. Any data obtained by any method or technique has to be analyzed statistically to evaluate the significance of the results. That means calculating the mean of a number of experiments and determine the standard deviation (or standard error) of the mean and analyze whether the differences observed between groups are statistically significant. Just looking at the data obtained and coming to a conclusion that the results are significant is deemed to be speculative. Furthermore, instant claims recite several members in each group of excipients, lubricants, disintegrants and inorganic base and the scope of the claims is not commensurate with the results obtained with lactose or mannitol. Finally it should be pointed out that the degradation values of the active agent observed with different excipients are so low and since the excipients, lubricants and disintegrants are known in tabletting technology and the prior is suggestive of these agents, selecting the proper excipient, lubricant, disintegrating agent and an inorganic base to obtain the best suited combination for that particular active agent is deemed to be within the skill of the art. The rejections thus, are maintained.

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/G S Kishore/

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK